
Cellular therapies supplement: the peritoneum as an ectopic site of hematopoiesis following in utero transplantation.

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Public Summary:

Human inherited diseases could possibly be cured for life if the patient received, and did not reject, healthy precursor cells specific for his disease. This cell transfer or transplantation treatment can occur in utero before a baby is even born. In this study, we inserted human blood-precursor cells into the abdominal cavity of mice with the aim of finding human blood cells now being made inside the mouse such that the mouse's body no longer rejects a foreign human skin graft. We found that the blood precursor cells remained in the mouse's abdominal cavity for months after transplant, fortifying the idea that this cavity can be a useful site for effective transplantation.

Scientific Abstract:

BACKGROUND: In utero transplantation (IUT) has the potential to treat birth defects early before full development of the immune system. Relatively small grafts, which are not matched for major histocompatibility antigens, can be delivered even before onset of disease symptoms. IUT of hematopoietic stem cells is usually performed via intraperitoneal injection, yet the fate of donor cells in the peritoneal cavity is not fully understood. We review our recent work and present new data demonstrating that the peritoneum can be a site of ectopic hematopoiesis with implications for IUT and immune tolerance induction. **STUDY DESIGN AND METHODS:** Haplogeneic and allogeneic fetal transplants were performed in mice and engraftment tracked by flow cytometry. Immune tolerance was studied by mixed lymphocyte reactions and skin transplantation. Adult syngeneic murine transplants and xenogeneic human into immunodeficient mouse transplants were performed to follow hematopoietic retention in the peritoneum and engraftment of the marrow. **RESULTS:** Although most transplanted cells rapidly clear the peritoneum, hematopoietic cells and cells with the phenotype of hematopoietic precursors can remain in the peritoneal cavity for months after transplant. The presence of donor cells in the peritoneum can contribute to donor-specific tolerance, but sufficient peripheral blood chimerism is required to ensure acceptance of donor skin grafts. **CONCLUSION:** Ectopic hematopoiesis and the survival of stem cells in the peritoneum offer the possibility of better using the peritoneal cavity to delivery stem cells and foster the development of immune tolerance to alloantigens or other foreign antigens.

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